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Heamato biochemical evaluation of induction combinations of romifidine guaifenesin ketamine and dexmedetomidine guaifenesin ketamine under isoflurane anesthesia in cattle

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Abstract
The study was conducted to evaluate the feasibility of romifidine and dexmedetomidine sedation for guaifenesin, ketamine-isoflurane general anaesthesia for various surgeries in cattle. The study was carried out in 12 clinical cases of cattle presented to Veterinary Clinical Complex, Veterinary College Bidar for various surgical procedures. The cases were randomly divided into two groups consisting of six cattle in each group. The animals of group I were administered with romifidine (10 µg/kg, IV). The animals of group II were administered with dexmedetomidine hydrochloride (2.5µg/kg, IV) immediately followed by guaifenesin (50 mg/kg, 5% sol). After ten minutes, the anaesthesia was induced by administering ketamine hydrochloride (3 mg/kg, I/V) and maintained with isoflurane (1-2%) in both the groups. Though the induction and recovery were smooth and uneventful in both groups, faster onset of sedation, faster down time to sternal recumbency, early recovery time to regain sternal position and to assume standing position were noticed in cattle premedicated with romifidine than in cattle premedicated with dexmedetomidine for guaifenesin-ketamine-isoflurane general anaesthesia Haemoglobin, packed cell volume, total erythrocyte count and total leukocyte count decreased non-significantly at maximum depth of anaesthesia in both the groups. Neutrophilia and relative lymphocytopenia was recorded in both the groups. Biochemical parameters decreased significantly towards the end of anaesthetic period in both the groups, however, it was within normal physiological limits. The present study showed romifidine-guaifenesin-ketamine-isoflurane combination was ideal to perform major surgeries in cattle without any haemato biochemical parameters complications.

Keywords: haemato biochemical, romifidine, dexmedetomidine, anesthesia

1. Introduction
General anaesthesia in cattle involves complexities like regurgitation, bloat, respiratory complication, nerve paralysis etc., which are not often encountered in small animals however, carefully selected and properly managed general anaesthetic technique provide optimal conditions for surgery.

In recent years, intravenous anaesthetics with rapid onset, redistribution and clearance have become available, which creates the possibility of maintaining anaesthesia even in large ruminants using these intravenous agents (Malik *et al.*, 2012) [7]. Moreover, the use of intravenous anaesthetic agents for induction and maintenance of anaesthesia may facilitate endotracheal intubation, oxygen administration or artificial ventilation if it is required.

Cattle and buffaloes usually accept physical restraint well and that to in conjuction with local or regional anaesthesia is often sufficient for completion of many surgical procedures. However, many times in non co-operative animals and in diagnostic and surgical procedure that are more complex like, diaphragmatic hernia, traumatic pericarditis and orthopedic surgeries where technical and anatomical aspects of the surgical procedures warrant absolute control of movement during surgery (Kumar *et al.*, 2013) [6]. General anaesthesia is required in cattle and buffaloes for complex surgical or diagnostic procedures. Inhalation anaesthesia requires specific equipment and may only be possible in the hospital environment. It is rarely feasible for use in the field.

Romifidine is a drug that is used in veterinary medicine as a sedative mainly in large animals such as horses, although it may be used in a wide variety of species. It is not used in humans, however is closely related in structure to the commonly used drug clonidine. Romifidine acts as an agonist at the α_2 adrenergic receptor subtype.

Side effects include bradycardia and respiratory depression. It is often used alongside other sedative or analgesic drugs such as ketamine or butorphanol and yohimbine can be used as an antidote to rapidly reverse the effects.

Materials and Methods

The study was conducted in 12 clinical cases presented to Veterinary Clinical Complex, Bidar. The study was conducted to evaluate induction combinations romifidine- guaifenesin-ketamine and dexmedetomidine-guaifenesin-ketamine under isoflurane anaesthesia in cattle. All the animals in Group-I (R) received romifidine intravenously, at the dose rate of 10 µg/kg body weight. Immediately after administration of romifidine, guaifenesin as 5 percent solution in normal saline at the dose rate of 50 mg/kg body weight intravenously was administered. After 5 minutes the animals were restrained in lateral recumbency and general anaesthesia was induced by administering ketamine at the dose rate of 3mg/kg body weight intravenously.

In the Group-II, dexmedetomidine was administered at the dose rate of 2.5 µg/kg body weight intravenously, immediately after administation of dexmedetomidine, guaifenesin as 5 percent solution in normal saline at the dose rate of 50 mg/kg body weight intravenously was administered. After 5 minutes the animals were restrained in lateral recumbency and general anaesthesia was induced by administering ketamine at the dose rate of 3mg/kg body weight intravenously. Dosages of drugs used in both the groups were determined based on clinical trials and previous literature and maintained with isoflurane (1-2%) in both the groups. Hematological parameters such as, hemoglobin, packed cell volume, Total erythrocyte count, Total leukocyte count, neutrophills and lymphocytes was recorded before premedication (0 minute), 10 minutes after premedication and at 5, 15, 30, 60 and 120 minutes after induction of general anesthesia. Biochemical parameters like, Alanine transaminase, Aspartate transaminase Serum creatinine and Serum urea nitrogen was recorded before pre-medication (0 minutes) and 10 minutes after premedication and at, 5, 15, 30, 60 and at 120 minutes interval after induction of general anaesthesia.

Results and Discussion

This study was undertaken to see the hematological and biochemical effect by using romifidine at 10 µg/kg body weight given intravenously (Group I) and dexmedetomidine hydrochloride at 2.5 µg/kg body weight given intravenously (Group II) for guaifenesin-ketamine-isoflurane general anaesthesia in cattle undergoing clinical surgeries. The results of the study were evaluated and discussed under following headings.

Hematological observations

Haemoglobin value fluctuated within normal physiological limits in both the groups and there was no significant difference between the groups at any intervals of the study. The haemoglobin level decreased non-significantly at 10 minutes after premedication in both the groups. The decreased haemoglobin has been reported after administration of dexmedetomidine in dogs (Gupta, 2010) [2] and sheep (Monsang, 2011) [8]. Singh *et al.* (2013) [9] reported decreased haemoglobin in buffaloes premedicated with dexmedetomidine and fentanyl. The decrease in haemoglobin during anaesthesia may be caused by the shifting of fluid from the extravascular compartment in order to maintain normal cardiac output (Wagner *et al.*, 1991) [12]. There was no significant difference in packed cell volume between the groups at all the intervals of study. Packed cell volume decreased non-significantly at 10 minutes after premedication in both the groups. The packed cell volume decreased significantly at 30 and 60 minutes during guaifenesin-ketamine-isoflurane anaesthesia in both the groups. Hikasa *et al.* (2000) reported a decrease in packed cell volume in sheep under isoflurane anaesthesia and up to 3 days post anaesthesia. The decrease in packed cell volume may be probably due to the stress caused by the sedative drugs (Bollwahn *et al.*, 1970), decreased heart rate and blood pressure (Khamis and Selah, 1970) and hemodilution by infiltration of interstitial fluids during anaesthesia. The total erythrocyte count decreased non-significantly at 30 minutes after premedication in both the groups. The total erythrocyte count decreased significantly from 30 to 120 minutes during guaifenesin-ketamine-isoflurane anaesthesia in both the groups. The comparison between the groups at different intervals did not reveal significant difference in the total erythrocyte count. Kumar *et al.* (2001) [5] observed a significant decrease in total erythrocyte count in dogs administered with haloperidol and ketamine. Monsang (2011) [8] observed a decrease in total erythrocyte count after injecting dexmedetomidine in sheep. Hikasa *et al.* (2000) [3] reported a decrease in total erythrocyte count in sheep under isoflurane anaesthesia. The total leukocyte count decreased between at 30 to 60 minutes in cattle of both groups throughout the study. However, the comparison between the groups at different intervals did not reveal significant difference in the total leukocyte count. A significant decrease in total leukocyte count was reported after administration of dexmedetomidine in sheep (Monsang, 2011) [8] and horses (Wagner *et al.*, 1991) [12]. Kumar *et al.* (2001) [5] observed a significant decrease in total leukocyte count from 5 to 45 minutes during haloperidol- ketamine anaesthesia in dogs. A significant increase in neutrophils with a subsequent significant decrease in lymphocytes was observed under ketamine-isoflurane anaesthesia in cattle of group I from 30 to 120 minutes and in cattle of group II at 30 and 60 minutes (Venkatgiri, 2017) [11] (Table 1 and 2).

Biochemical observations

The serum alanine transaminase and serum aspartate transaminase increased significantly at 120 minutes after administration of guaifenesin-ketamine-isoflurane anaesthesia in both the groups. There was no significant difference between the groups at all the intervals of the study. Topal *et al.* (2003) [10] reported increased alanine transaminase activities two days after isoflurane anaesthesia in dogs. However, Hikasa *et al.* (2000) [3] reported non-significant alteration in alanine transaminase during and up to three days after isoflurane anaesthesia in sheep. Serum creatinine did not alter significantly throughout the anaesthetic period in both the groups. Similar findings were observed by Hikasa *et al.* (2000) [3] after isoflurane anaesthesia in sheep. The serum urea nitrogen increased significantly at 60 and 120 minutes in both the group of animals. Singh *et al.* (2013) [9] reported a significant increase in urea nitrogen in buffaloes anaesthetized with xylazine-fentanyl-thiopentone-isoflurane and dexmedetomidine- fentanyl-thiopentone-isoflurane (Table 3). In conclusion hematobiochemical parameters though changed significantly during general anaesthesia in both the groups, it was within normal range and was only transient, not alarming to suggest any pathological condition.

Table 1: Mean ± S.E of hematological parameters at different intervals in cattle of Group I and II

Sl. No.	Parameter	Time Intervals		Group I	Group II
		0 min		15.61 ± 0.25	15.86 ± 0.38
		After	**10 min**	14.87 ± 0.68	15.24 ± 0.79
1	Haemoglobin (g/dL)	premedication Afterguaifenesin-ketamine - isoflurane administration	30 min	14.37 ± 0.67	14.66 ± 0.95
			60 min	14.98 ± 0.53	14.76 ± 0.63
			120 min	14.72 ± 0.68	14.92 ± 0.59
		0 min		40.85 ± 1.17	40.63 ± 1.21
2	Packed Cell Volume (%)	After premedication Afterguaifenesin- ketamine - isoflurane administration	10 min	40.38 ± 0.68	40.57 ± 1.53
			30 min	40.43 ± 1.50	39.98 ± 0.99
			60 min	39.83 ± 1.22	39.52 ± 0.88
			120 min	39.92±0.98	39.23 ± 1.33
		0 min		7.45 ± 0.54	7.84 ± 0.88
4	Total Erythrocyte Count (×106/µL)	After premedication Afterguaifenesin-ketamine - isoflurane administration	10 min	7.12 ± 0.81	7.43 ± 0.66
			30 min	6.85 ± 0.75	6.86 ± 0.73
			60 min	6.98 ± 0.74	7.05 ± 0.15
			120 min	7.39 ± 0.71	7.21 ± 0.85
		0 min		12.74 ± 0.79	12.26 ± 0.65
5	Total Leukocyte Count (103/µL)	After premedication Afterguaifenesin-ketamine - isoflurane administration	10 min	12.52 ± 0.63	11.87 ± 0.39
			30 min	11.96 ± 0.38	11.56 ± 0.28
			60 min	11.39 ± 0.61	11.34 ± 0.27
			120 min	10.97 ± 0.91	11.67 ± 0.75

Means bearing superscript* differ significantly (*P≤0.05*) from interval 'before' within the group Means bearing superscript** differ significantly (*P≤0.01*) from interval 'before' within the group

Table 2: Mean ± S.E of differential leukocyte count at different intervals in Group I and II

Sl. No.	Parameter	Time Intervals		Group I	Group II
		0 min		36.00 ± 0.43	36.17 ± 1.02
		After	**10 min**	37.61 ± 1.63	38.33 ± 1.63
1	Neutrophils (%)	premedication After Ketamine-guaifenesin - isoflurane administration	30 min	40.30 ± 0.91**	43.37 ± 0.29**
			60 min	37.11 ± 0.27**	34.83 ± 0.61**
			120 min	36.17 ± 0.92**	36.33 ± 0.41**
		0 min		61.83 ± 1.07	61.17 ± 1.91
		After	10 min	59.40 ± 1.31	60.33 ± 1.12
2	Lymphocytes (%)	premedication ketamine- guaifenesin - isoflurane administration	30 min	55.49 ± 0.24**	58.67 ± 1.15*
			60 min	57.15 ± 1.35*	59.37 ± 0.37*
			120 min	58.39 ± 0.72	60.97 ± 1.15
		0 min		2.13 ± 0.41	2.83 ± 0.32
		After	10 min	2.11 ± 0.19	2.40 ± 0.51
3	Monocytes (%)	premedication ketamine- guaifenesin - isoflurane administration	30 min	2.97 ± 0.41	2.33 ± 0.38
			60 min	2.50 ± 0.14	1.93 ± 0.81
			120 min	2.83 ± 0.91	2.37 ± 0.81
		0 min		1.91 ± 0.81	1.89 ± 0.61
		After			
4	Eosinophils (%)	premedication ketamine- guaifenesin - isoflurane administration	10 min	1.77 ± 0.38	1.70 ± 0.56
			30 min	1.93 ± 0.31	1.63 ± 0.51
			60 min	2.11 ± 0.43	1.77 ± 0.64
			120 min	2.43 ± 0.57	1.87 ± 0.82

Means bearing superscript* differ significantly (*P≤0.05*) from interval 'before' within the group Means bearing superscript** differ significantly (*P≤0.01*) from interval 'before' within the group Basophil count in both the groups at all the intervals was '0'

Table 3: Mean ± S.E of biochemical parameters at different intervals in cattle of group I and II

Parameters	Groups	0 min	After premedication	After ketamine-isoflurane administration	
			10 min	60 min KI	120 min KI
ALT (IU/L)	Group I	27.13±1.38	26.40±0.96	27.83±0.52	28.67±0.98
	Group II	26.77±0.98	25.13±1.75	27.37±1.57	27.50±1.72
AST (IU/L)	Group I	93.83±1.33	95.48±2.32	100.67±2.07	106.50±2.61
	Group II	91.67±2.54	93.70±3.11	94.33±2.01	96.17±2.46
Serum creatinine (mg/dL)	Group I	1.17±0.12	1.32±0.43	1.47±0.71	1.56±0.83
	Group II	1.54±0.15	1.57±0.87	1.68±0.32	1.75±0.20
Serum urea nitrogen (mg/dL)	Group I	18.19±1.51	19.43±1.49	22.81±0.54	24.74±1.12
	Group II	15.96±1.02	14.01±1.08	18.18±1.21	20.53±1.66

Conclusion

The present study showed romifidine-guaifenesin-ketamine-isoflurane combination was ideal to perform major surgeries in cattle without any complications. However, dexmedetomidine hydrochloride as a premedication for guaifenesin-ketamine-isoflurane anaesthetic combination was less optimum at this given dose in cattle.

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